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Capecitabine in Advanced Gastric or Oesophagogastric Cancer

A Viewpoint by Sai-Hong Ignatius Ou and Randall F. Holcombe

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Oral formulations of antineoplastic drugs are becoming a mainstay in oncology and haematology. Capecitabine is an oral prodrug of fluorouracil that is activated via a three-step enzymatic process and has the advantage of being preferentially concentrated in tumours. Capecitabine is approved for the treatment of patients with stage III colon cancer, first-line treatment of metastatic colon cancer and the treatment of metastatic breast cancer (either as a single agent for patients whose disease is resistant to paclitaxel and anthracyclines, or in combination with docetaxel after failure on anthracycline-based therapy). The US FDA-approved dosage of capecitabine is 1250 mg/m^2 twice daily for 14 days in a 3-week cycle. However, this recommended dosage is often associated with the adverse effects of hand-foot syndrome, stomatitis, diarrhoea and myelosuppression.

Phase II combination trials in upper GI malignancies have used capecitabine at a dose range from 1000 to 1250 mg/m^2 twice daily for 14 days in a 3-week cycle. Dosage reductions were required in 35-63% of the cases that utilised the approved 1250 mg/m^2 twice daily dosage. Phase I dose escalation of capecitabine combinations in upper GI malignancies found the optimal dosage to be 1000 mg/m^2 twice daily for 14 days in a 3-week cycle.[1] Phase III randomised trials of capecitabine have utilised a dosage of 1000 mg/m^2 twice daily for 14 days every 3 weeks or 625 mg/m^2 twice daily continuously in a 3-week cycle. Using these dosage regimens, the efficacy of capecitabine seems to be preserved and toxicities were well tolerated.

Regarding efficacy, capecitabine appears equivalent to intravenous fluorouracil in patients with gastric and oesophagogastric cancers. The toxicity profile is somewhat distinct but overall the two agents have similar tolerability. The oral route of administration of capecitabine is the primary advantage.

Identifying patients who are most likely to respond to treatment or develop significant toxic effects is essential. The ratio of thymidine phosphorylase (TP) to dihydropyrimidine dehydrogenase (DPD) within the tumour may provide useful information. In one study, patients with a high TP **:** DPD (>1.9) and who received oral deoxy-5-fluorouridine had a significantly improved response rate and median survival.[2]

Finally, other oral fluoropyrimidine compounds such as UFT (tegafur + uracil) and S-1 (tegafur + 5′-chloro-2, 4-dihydroxypyridine + uracil) are being investigated in advanced gastric and oesophagogastric cancers. Future comparison of these compounds with capecitabine in terms of efficacy and toxicity are warranted. ▲

References

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